1636

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

The the Application of

Derek van der Kooy, t. al.

MAY 2 8 2003

Application No.

09/966, 768

TECH CENTER 1600/2900

Attorney Docket No.

Bereskin & Parr

JECH GEHTER 1600/2900

Filed:

MAY 2 7 2003

September 28, 2001

For:

PRIMITIVE NEURAL STEM CELLS AND

METHOD FOR DIFFERENTIATION OF STEM

**CELLS TO NEURAL CELLS** 

Examiner:

Daniel M. Sullivan

**Group Art Unit:** 

1636

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INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97

In compliance with the duty of disclosure set forth in 37 C.F.R. § 1.56, Applicants are submitting herewith a Form PTO-1449 and a copy of the references listed thereon. This Information Disclosure Statement is being filed more than three months after the filing date of this application, and after receipt of the first Official Action on the merits, but before receipt of a Final Official Action or a Notice of Allowance. Accordingly, the fee required under 37 C.F.R. 1.97(c) is enclosed. In the event the check is improper, or the fee calculation is in error, the Commissioner is authorized to charge any underpayment or credit any overpayment to the account of the undersigned attorneys, Account No. 04-1406. A duplicate copy of this sheet is enclosed.

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In the opinion of the undersigned, the references submitted herewith are the most pertinent of which the undersigned is aware. However, no representation is made or intended that more pertinent references do not exist.

This submission is not an admission that the references listed on the attached Form PTO-1449 constitute prior art against the claims of this application.

The Examiner is respectfully requested to confirm receipt and consideration of the cited references by initialing and returning a copy of the attached Form PTO-1449 in accordance with MPEP §609.

Early and favorable consideration of this application is respectfully requested.

Respectfully submitted,

DANN, DORFMAN, HERRELL & SKILLMAN A Professional Corporation Attorneys for Applicant(s)

> Kathleen D. Rigaut, Ph.D, J.D. PTO Registration No. 43,047

Telephone: (215) 563-4100 Facsimile: (215) 563-4044 Enclosures - Form PTO-1449

Copies of references listed on PTO - 1449

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Application Number 09/966,768
Filing Date September 28, 2001
First Named Inventor Derek van der Kooy
Group Art Unit 1636
Examiner Name Daniel M. Sullivan

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Sheet 1 of 9 Attorney Docket Number Bereskin & Parr

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Initials*	No.1	Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Applicant of Cited Document	Passages or Relevant Figures Appear	T⁰	
		WO 99/01553 A	Jan 14, 1999	Genetics Institute, University of California			
		WO 99/01159 A	Jan 14, 1999	University of Utah Research Foundation			
		WO 01/51616 A2	July 19, 2001	Geron Corporation			
		WO 99/32606 A	July 1, 1999	Brüstle, Oliver			

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		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS TECH CENT	(ER 16
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		Y. Benninger et al. "Differentiation and Histological Analysis of Embryonic Stem Cell-Derived Neural Transplants in Mice." Brain Pathology 10 pp 330-341 (2000).	
		I L. Weissman. "Translating Stem and Progenitor Cell Biology to the Clinic: Barriers and Opportunities. Science, Vol. 287, February 25, 2000.	
		P.J. Donovan & J. Gearhart. "The end of the beginning for pluripotent stem cells." Nature, Vol. 414, November 1, 2001, pp 92-97.	
		C.H. Waddington and G.A. Schmidt. "Induction by Heteroplastic Grafts of the Primitive Streak in Birds." Roux's Arch. EntwMech. Org. 128, (1933) pp 522-563.	
		G. R. Martin et al. "The Development of Cystic Embryoid Bodies in Vitro from Clonal Teratocarcinoma Stem Cells." Developmental Biology 61, pp 230-244 (1977).	
		R.S.P Beddington and E.J. Robertson. "An assessment of the developmental potential of embryonic stem cells in the midgestation mouse embryo." Development 105, (1989) pp 733-737.	
		J.M. Oppenheimer. "Structures Developed in Amphibians by Implantation of Living Fish Organizer." Proc. Soc. Exp. Biol. Med. 34, (1936) pp 461-463.	
		H. Spemann and H. Mangold. "Über Induktion von Embryonalanlagen durch Implantation artfremder Organizatoren." Arch. Mikr. Anat. EntwMech. 100, (1924) pp 599-639.	
		M.V. Wiles and B. M. Johansson. "Analysis of Factors Controlling Primary Germ Layer Formation and Early Hematopoiesis Using Embryonic Stem Cell in Vitro Differentiation." Leukemia 11 (S3)m (1997) pp 454-456.	
		B.A. Reynolds et al. "A Multipotent EGF-Responsive Striatal Embryonic Progenitor Cell Produces Neurons and Astrocytes." The Journal of Neuroscience, November 1992 12(11), pp 4565-4574.	
		J. Nichols et al. "Derivation of Germline Competent Embryonic Stem Cells with a Combination of Interleukin-6 and Soluble Interleukin-6 Receptor." Experimental Cell Research 215, pp 237-239 (1994).	
		M.J. Evans and M.H. Kaufman. "Establishment in culture of pluripotential cells from mouse embryos." Nature, Vol. 292, July 9, 1981, pp 154-156.	
		A. Nagy and J. Rossant. "Production of completely ES cell-derived fetuses." In Gene targeting: a practical approach (ed. A.L. Joyner), pp 147-179, IRL Press, Oxford, UK.	
		C.G. Bellows and J.E. Aubin. "Determination of Numbers of Osteoprogenitors Present in Isolated Fetal Rat Calvaria Cells in Vitro." Developmental Biology 133, pp 8-13 (1989).	
		H. Kawasaki et al. "Induction of midbrain dopaminerigc neurons from ES cells by stromal cell-derived inducing activity." Neuron 28, pp 31-40.	

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		J.J. Otero et al. "Cell-cell contact regulates commitment by cultured embryonic stem cells." Society for Neuroscience Abstracts, Vol. 27, No. 1, p 341, 2001.	
		S. Taraviras et al. "Characterization of the mouse HNF-4 gene and its expression during mouse embryogenesis." Mechanisms of Development 48 (1994) pp 67-79.	
		M. Li et al. "Essential function of LIF receptor in motor neurons." Nature, vol. 378, Dec 14, 1995, pp 724-727.	
		Y. Nakamura et al. "The bHLH Gene <i>Hes1</i> as a Repressor of the Neuronal Commitment of CNS Stem Cells." The Journal of Neuroscience, Jan 1, 2000, 20(1) pp 283-293.	
		D. Martens et al. "Separate Proliferation Kinetics of Fibroblast Growth Factor-Responsive and Epidermal Growth Factor-Responsive Neural Stem Cells within the Embryonic Forebrain Germinal Zone." The Journal of Neuroscience, Feb 1, 2000, 20(3), pp 1085-1095.	
		A. Fainsod et al. "The dorsalizing and neural inducing gene <i>follistatin</i> is an antagonist of <i>BMP-4</i> ." Mechanisms of Development 63 (1997), pp 39-50.	
		S. Weiss et al. "Is there a neural stem cell in the mammalian forebrain?" TINS Vol. 19, No. 9, 1996, pp 387-393.	
		R. Harland and J. Gerhart. "Formation and Function of Spemann's Organizer." Annu. Rev. Cell Dev. Biol., 1997, 13 pp 611-667	
		J. Conover et al. "Ciliary neurotrophic factor maintains the pluripotentiality of embryonic stem cells." Development 119, pp 559-565 (1993).	
		G. R. Martin. "Isolation of a pluripotent cell line from early mouse embryos cultured in medium conditioned by teratocarcinoma stem cells." Proc. Natl. Acad. Sci. USA, Vol. 78, No. 12, pp. 7634-7638, December 1981,	
		A. Nagy et al. "Derivation of completely cell culture-derived mice from early-passage embryonic stem cells." Proc. Natl. Acad. Sci. USA, Vol. 90, no. 18, pp 8424-8428, September 1993.	
		T. Lamb et al. "Neural Induction by the Secreted Polypeptide Noggin." Science Vol. 262, Oct 29, 1993, pp 713-718.	
		B. Reynolds and S. Weiss. "Generation of Neurons and Astrocytes from Isolated Cells of the Adult Mammalian Central Nervous System." Science, Vol. 255, pp 1707-1710, March 1992.	
		D. van der Kooy and S. Weiss. "Why Stem Cells?" Science Vol. 287, Feb 25, 2000, pp 1439-1441.	
		R. L. Williams et al. "Myeloid leukaemia inhibitory factor maintains the developmental potential of embryonic stem cells." Nature Vol. 336, Dec. 15, 1988, pp 684-687.	

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		D. G. Wilkinson et al. "Segmental expression of Hox-2 homoeobox-containing genes in the developing mouse hindbrain." Nature Vol. 341, Oct. 5, 1989, pp 405-409.	
		W. S. Smith et al. "Secreted <i>noggin</i> protein mimics the Spemann organizer in dorsalizing <i>Xenopus</i> mesoderm." Nature vol. 361, Feb 11, 1993, pp 547-549.	
		A. Simeone et al. "Nested expression domains of four homeobox genes in developing rostral brain." Nature Vol. 358, Aug 20, 1992, pp 687-690.	
		Y. Sasai et al. "Regulation of neural induction by the Chd and Bmp-4 antagonistic pattering signals in <i>Xenopus</i> ." Nature Vol. 376, July 27, 1995, pp 333-336.	
		A. Hemmati-Brivanlou & D. A. Melton. "A truncated activin receptor inhibits mesoderm induction and formation of axial structures in <i>Xenopus</i> embryos." Nature Vol. 359, Oct. 15, 1992, pp 609-614.	
		P. A. Hoodless and A. Hemmati-Brivanlou. "Inhibitory control of neural differentiation in mammalian cells." Dev. Genes Evol (1997) 207 pp 19-28.	
		P.A. Wilson et al. "Concentration-dependent pattering of the <i>Xenopus</i> ectoderm by BMP4 and its signal transducer Smad1." Development 124, pp 3177-3184 (1997).	
		G. Oliver et al. "Six3, a murine homologue of the sine oculis gene, demarcates the most anterior border of the developing neural plate and is expressed during eye development." Development 121, pp 4045-4055 (1995).	
		Y. Grinblat et al. "Determination of the zebrafish forebrain: induction and patterning." Development 125, pp 4403-4416 (1998).	
		J. L. de la Pompa et al. "Conservation of the Notch signaling pathway in mammalian neurogenesis." Development 124, pp 1139-1148 (1997).	
		B. G. Ciruna et al. "Chimeric analysis of fibroblast growth factor receptor-1(Fgfr1) function: a role for FGFR1 in morphogenetic movement through the primitive streak." Development 124, pp 2829-2841 (1997).	
		D. Acampora et al. "Visceral endoderm-restricted translation of <i>Otx1</i> mediates recovery of <i>Otx2</i> requirements for specification of anterior neural plate and normal gastrulation." Development 125, pp 5091-5104 (1998).	
		R.S.P. Beddington. "Induction of a second neural axis by the mouse node." Development 120, pp 613-620, (1994).	
		R.S.P. Beddington et al. "Brachyury – a gene affecting mouse gastrulation and early organogenesis." Development 1992 Supplement, pp 157-165 (1992).	
		T.P. Yamaguchi et al. "fgfr-1 is required for embryonic growth and mesodermal patterning during mouse gastrulation." Genes & Development 8, pp 3032-3044, 1994.	

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		J. Li et al. "Mammalian hepatocyte differentiation requires the transcription factor HNF-4α." Genes & Development 14, pp 464-474, 2000.	
		S. Hoppler et al. "Expression of a dominant-negative Wnt blocks induction of MyoD in <i>Xenopus</i> embryos." Genes & Development 10, pp 2805-2817, 1996.	
		G. Friedrich and P. Soriano. "Promoter traps in embryonic stem cells: a genetic screen to identify and mutate developmental genes in mice." Genes & Development 5, pp 1513-1523, 1991.	
		V. Tropepe et al. "Distinct Neural Stem Cells Proliferate in Response to EGF and FGF in the Developing Mouse Telencephalon." Developmental Biology 208, pp 166-188, 1999.	
		B.A. Reynolds and S. Weiss. "Clonal and Population Analyses Demonstrate That an EGF-Responsive Mammalian Embryonic CNS Precursor Is a Stem Cell." Developmental Biology 175, pp 1-13, 1998.	
		J.L. Wrana. "Regulation of Smad Activity." Cell, Vol. 100, pp 189-192, Jan 21, 2000.	
		U. Lendahl et al. "CNS Stem Cells Express a New Class of Intermediate Filament Protein." Cell, Vol. 60, pp 585-595, February 23, 1990.	
		G. Bain et al. "Embryonic Stem Cells Express Neuronal Properties in Vitro." Developmental Biology 168, pp. 342-357 (1995).	
		S. Okabe et al. "Development of neuronal precursor cells and functional postmitotic neurons from embryonic stem cells in vitro." Mechanisms of Development 59 (1996), pp 89-102.	
		S. Piccolo et al. "Dorsoventral Patterning in Xenopus: Inhibition of Ventral Signals by Direct Binding of Chordin to BMP-4." Cell, Vol. 86, pp 589-598, August 23, 1996.	
		L.B. Zimmerman et al. "The Spemann Organizer Signal noggin Binds and Inactivates Bone Morphogenetic Protein 4." Cell, Vol. 86, 599-606, August 23, 1996.	
		E. Coucouvanis and G.R. Martin. "BMP singaling plays a role in visceral endoderm differentiation and cavitation in the early mouse embryo." Development 126, pp 535-546, (1999).	
		S. Piccolo et al. "The head inducer Cerberus is a multifunctional antagonist of Nodal, BMP and Wnt signals." Nature Vol. 397, Feb 25, 1999, pp. 707-710.	***************************************
		J.J.H. Pearce et al. "A Mouse Cerberus/Dan-Related Gene Family." Developmental Biology 209, pp 98-110 (1999).	
		A. Streit and C.D. Stern. "Neural induction a bird's eye view." TIG, January 1999, Vol. 15, No. 1, pp 20-24.	

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		A. Streit et al. "Chordin regulates primitive streak development and the stability of induced neural cells, but is not sufficient for neural induction in the chick embryo." Development 125, pp 507-519 (1998).	
		H. Grunz and L. Tacke. "Neural differentiation of <i>Xenopus laevis</i> ectoderm takes place after disaggregation and delayed reaggregation without inducer." Cell Differentiation and Development, 28 (1989), pp 211-218.	
		C. Sirard et al. "The tumor suppressor gene Smad4/Dpc4 is required for gastrulation and later for anterior development of the mouse embryo." Genes & Development 12, pp 107-119, 1998.	
		J. A. Belo et al. "Cerberus-like is a secreted factor with neuralizing activity expressed in the anterior primitive endoderm of the mouse gastrula." Mechanisms of Development 68 (1997) pp 45-57.	
		S. M. Sato and T. D. Sargent. "Development of Neural Inducing Capacity in Dissociated <i>Xenopus</i> Embryos." Developmental Biology 134, pp 263-266 (1989).	
		B. M. Johansson and M. V. Wiles. "Evidence for Involvement of Activin A and Bone Morphogenetic Protein 4 in Mammalian Mesoderm and Hematopoietic Development." Molecular and Cellular Biology, Jan 1995, pp 141-151.	
		P. A. Wilson and A. Hemmati-Brivanlou. "Induction of epidermis and inhibition of neural fate by Bmp-4." Nature, Vol. 376, July 27, 1995, pp 331-336.	
		S.F. Godsave and J.M. W. Slack. "Single cell analysis of mesoderm formation in the Xenopus embryo." Development 111, pp 523-530 (1991).	
		A. Glinka et al. "Head induction by simultaneous repression of Bmp and Wnt signaling in <i>Xenopus</i> ." Nature, Vol. 389, October 2, 1997, pp 517-519.	
		A. Hemmati-Brivanlou and D. Melton. "Vertebrate Neural Induction." Annu. Rev. Neurosci., 1997, 20, pp 43-60.	
		M. F. A. Finley et al. "BMP-4 Inhibits Neural Differentiation of Murine Embryonic Stem Cells." Jon Wiley & Sons, Inc. J. Neurobiol 40, pp 271-287, 1999	
		D. Bachiller at al. "The organizer factors Chordin and Noggin are required for mouse forebrain development." Nature, Vol. 403, February 10, 2000, pp 658-661.	
		T. Bouwmeester et al. "Cerberus is a head-inducing secreted factor expressed in the anterior endoderm of Sepmann's organizer." Nature, Vol. 382, August 15, 1996, pp 595-601.	
		T. Tohyama et al. "Nestin Expression in Embryonic Human Neuroepithelium and in Human Neuroepithelial Tumor Cells." Laboratory Investigation, Vol. 66, No. 3, pp 303-313, 1992.	
		S. Fedoroff et al. "Microglia and Astroglia Have a Common Progenitor Cell." Journal of Neuroscience Research 50, pp 477-486 (1997).	

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 		I. L. Weissman. "Stem Cells: Units of Development, Units of Regeneration, and Units in Evolution." Cell, Vol. 100, pp 157-168, January 7, 2000.	
		S.J. Morrison et al. "Regulatory Mechanisms in Stem Cell Biology." Cell, Vol. 88, pp 287-298, February 7, 1997.	
		A. Simeone et al. "Two vertebrate homeobox genes related to the <i>Drosophila empty spiracles</i> gene are expressed in the embryonic cerebral cortex." The EMBO Journal, Vol. 11, No. 7, pp 2541-2550, 1992.	
		C.S. Potten and M. Loeffler. "Stem cells: attributes, cycles, spirals, pitfalls and uncertainties. Lessons for and from the Crypt." Development 110, pp 1001-1020 (1990).	
		D.L. Clarke et al. "Generalized Potential of Adult Neural Stem Cells." Science, Vol. 288, pp 1660-1663, June 2, 2000.	
		A. Hemmati-Brivanlou and D. A. Melton. "Inhibition of Activin Receptor Signaling Promotes Neuralization in Xenopus." Cell, Vol. 77, pp 273-281, April 22, 1994.	
		R. S. P. Beddington and E. J. Robertson. "Axis Development and Early Asymmetry in Mammals." Cell, Vol. 96, pp 195-209, January 22, 1999.	
		A. G. Smith et al. "Inhibition of pluripotential embryonic stem cell differentiation by purified polypeptides." Nature, Vol. 336, December 15, 1988, pp 688-690.	
		C. Strubing et al. "Differentiation of pluripotent embryonic stem cells into the neuronal lineage in vitro gives rise to mature inhibitory and excitatory neurons." Mechanisms of Development 53 (1995) pp 275-287.	
		A. Fraichard et al. " In vitro differentiation of embryonic stem cells into glial cells and functional neurons." Journal of Cell Science 108, pp 3181-3188 (1995).	
		W. L. Stanford et al. "Expression Trapping: Identification of Novel Genes Expressed in Hematopoietic and Endothelial Lineages by Gene Trapping in ES Cells." Blood, Vol. 92, No. 12, December 15, 1998, pp 4622-4631.	
		J. Nichols et al. "Formation of Pluripotent Stem Cells in the Mammalian Embryo Depends on the POU Transcription Factor Oct4." Cell, Vol. 95, pp 379-391, October 30, 1998.	
		U. Koshirnizu et al. "Functional requirement of gp130-mediated signaling for growth and survival of mouse primordial germ cells in vitro and derivation of embryonic germ (EG) cells." Development 122, pp 1235-1242, (1996)	
		C. Dani et al. "Paracrine Induction of Stem Cell Renewal by LIF-Deficient Cells: A New ES Cell Regulatory Pathway." Developmental Biology 203, pp 149-162 (1998).	
		A. G. Elefanty et al. "Hematopoietic-Specific Genes Are Not Induced During In Vitro Differentiation of sci-Null Embryonic Stem Cells." Blood, Vol. 90, No. 4, August 15, 1997; pp 1435-1447.	

Examiner	Date	
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Olgitature	Considered	

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

	Compl te if Known	
Application Number	09/966,768	
Filing Date	September 7, 200	1
First Named Inventor	Derek van der Koo	)Y
Group Art Unit	1636	RECEIV
Examiner Name	Daniel M. Sullivan	

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		R. J. Arceci, et al. "Mouse GATA-4: a Retinoic Acid-Inducible GATA-Binding Transcription Factor Expressed in Endodermally Derived Tissues and Heart." Molecular and Cellular Biology, April 1993, pp 2235-2246.	
		O.Brüstle et al. "Embryonic Stem Cell-Derived Glial Precursors: A Source of Myelinating Transplants." Science, Vol. 285, July 30, 1999, pp. 754—756.	
		M.George-Weinstein et al. "Skeletal Myogenesis: The Preferred Pathway of Chick Embryo Ephiblast Cells in Vitro." Developmental Biology 173, pp 279-291 (1996).	
		A-K. Hadjantonakis et al. "Generating green fluorescent mice by germline transmission of green fluorescent ES cells." Mechanisms of Development 76, (1998), pp 79-90.	
		M. F. Mehler and J.A. Kessler. "Hematolymphopoietic and inflammatory cytokines in neural development." TINS, Vol. 20, No. 8, 1997, pp 357-365.	
		T.C. Doetschman et al. "The <i>in vitro</i> development of blastocyst-derived embryonic stem cell lines: formation of visceral yolk sac, blood islands and myocardium." J. Embryol. exp. Mroph. 87, pp 27-45, (1985).	
		T. Kishimoto et al. "Cytokine Signal Transduction." Cell, Vol. 76, pp 253-262, January 28, 1994.	
		E. Coucouvanis and G. R. Martin. "Signals for Death and Survival: A Two-Step Mechanism for Cavitation in the Vertebrate Embryo." Cell, Vol. 83, pp 279-287, October 20, 1995.	
		B. J. Chiasson at al. "Adult mammalian forebrain ependymal and subependymal cells demonstrate proliferative potential but only subependymal cells have neural stem cell characteristics." J. Neurosci. 19, pp 4462-4471.	
		K.S. O'Shea. "Embryonic stem cell models of development." Anat. Rec. (New Anat.) 257, 32-41, 1999.	
		R.M. Seaberg et al. "Neural determination genes revealed by expression trapping in embryonic stem cells." Soc., Neurosci. Abst. 25, p 527, 1999.	
		J. Yamashita et al. "Fik1-positive cells derived from embryonic stem cells serve as vascular progenitors." Nature, Vol. 408, pp 92-96, Nov 2, 2000.	
		J. W. McDonald et al. "Transplanted embryonic stem cells survive, differentiate and promote recovery in injured rat spinal cord." Nature Medicine, Vol. 5, No. 12, pp 1410-1412, Dec 1999.	
		M. Yang et al. "Neural Stem Cells Spontaneously Express Dopaminergic Traits after Transplantation into the Intact or 6-Hydroxydopamine-Lesioned Rat." Experimental Neurology, Vol. 177, pp 50-60, 2002.	
		S. Weiss et al. "Multipotent CNS Stem Cells Are Present in the Adult Mammalian Spinal Cord and Venticular Neuroaxis." The Journal of Neuroscience, December 1, 1996, 16(23) pp 7599-7609.	

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	Complete if Known
Application Number	09/966,768
Filing Date	September 7, 2001
First Named Inventor	Derek van der Kooy
Group Art Unit	1636
Examiner Name	Daniel M. Sullivain
Attorney Docket Number	Bereskin & Parr

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	~ -
Examiner Initials *	Cite No.1	OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS  Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate) title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), voluments of number(s), publisher, city and/or country where published.	TER 160
		V. Tropepe et al. "Autonomous neural cell fate specification in mouse embryonic stem cells." Poster at Meeting of the Society for Neuroscience, Miami Beach, Florida, October 23-28, 1999.	

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